

Online Research @ Cardiff

This is an Open Access document downloaded from ORCA, Cardiff University's institutional repository: <https://orca.cardiff.ac.uk/id/eprint/124588/>

This is the author's version of a work that was submitted to / accepted for publication.

Citation for final published version:

Willcox, Darren and Melen, Rebecca L. ORCID: <https://orcid.org/0000-0003-3142-2831> 2019. Borane-catalyzed heterocycle synthesis. Trends in Chemistry 1 (6) , pp. 625-626. 10.1016/j.trechm.2019.06.011 file

Publishers page: <http://dx.doi.org/10.1016/j.trechm.2019.06.011>
<<http://dx.doi.org/10.1016/j.trechm.2019.06.011>>

Please note:

Changes made as a result of publishing processes such as copy-editing, formatting and page numbers may not be reflected in this version. For the definitive version of this publication, please refer to the published source. You are advised to consult the publisher's version if you wish to cite this paper.

This version is being made available in accordance with publisher policies.

See

<http://orca.cf.ac.uk/policies.html> for usage policies. Copyright and moral rights for publications made available in ORCA are retained by the copyright holders.



Borane-Catalyzed Heterocycle Synthesis

Darren Willcox¹ and Rebecca L. Melen^{1,*}

¹Cardiff Catalysis Institute, School of Chemistry, Cardiff University, Main Building, Park Place, Cardiff, CF10 3AT, UK

ORIGIN

Over the past few years, main group reagents (particularly Lewis acidic boranes) have garnered significant attention in synthetic bond-forming processes. Recently, tris (pentafluorophenyl)borane has been shown to activate C–C π -bonds, enabling synthesis of biologically active heterocyclic and aromatic compounds.

REACTION MECHANISM

The synthesis of heterocyclic and aromatic compounds can be achieved through borane-catalyzed activation of C–C π -bonds towards pendant nucleophiles. Recently, tris (pentafluorophenyl)borane [B(C₆F₅)₃] has been shown to exhibit unique properties, acting as either a hard Lewis acid with high oxophilic character or as a π -acid (analogous to gold) to activate alkynes. At the beginning of the catalytic cycle, free B(C₆F₅)₃ (I) is in equilibrium with the borane-carboxyl adduct (II). This was corroborated by the detection of a broad resonance in the ¹¹B NMR spectrum corresponding to the formation of this adduct. However, at an elevated temperature (70°C), decomplexation of B(C₆F₅)₃ from the carboxyl group occurs, followed by coordination to alkyne π -bond. This coordination facilitates a 6-endo-dig cyclization (formally a trans-1,2-oxyboration) furnishing (III). Formation of (III) was determined by the observation of a transient sharp singlet at approximately –15 ppm in the ¹¹B NMR spectrum characteristic of the formation of an alkenyl borate that can be isolated when R¹ = Me. Subsequent elimination of either a carbenium ion or proton [R¹]⁺ from the ester, followed by proto- or carbo-deboronation, yields the desired 3,4-dihydropyrone (IV) and releases B(C₆F₅)₃ to re-enter the catalytic cycle. While this transformation has been demonstrated for the synthesis of dihydropyrones and isocoumarins, the overall 1,2-oxoboration process is more general. As a result, a wide range of different heterocycles can be accessed in a facile manner, such as pyryliums, oxazoles, oxazolines, indoles, and dihydroquinolines, among others. All carbon scaffolds, such as polycyclic dibenzapentalenes, can also be accessed from a B(C₆F₅)₃-induced cyclization of 1,2-bis(phenylethynyl)benzenes.

*Correspondence: MelenR@cardiff.ac.uk (R.L. Melen).

IMPORTANCE

The use of a strong boron-based Lewis acid to promote catalytic cyclizations is a powerful metal-free approach leading to the formation of useful heteroaromatics and aromatics. This mechanism highlights the unique behavior of $\text{B}(\text{C}_6\text{F}_5)_3$ to act as both a hard Lewis acid and π -acid, and that divergent reactivity is possible employing $\text{B}(\text{C}_6\text{F}_5)_3$ as a catalyst. Borane-catalyzed reactions allow for the synthesis of high-value products in a sustainable manner, from cheap and readily available starting materials.

Literature

1. Soltani, Y. et al. (2017) Stoichiometric and catalytic C–C and C–H bond formation with $\text{B}(\text{C}_6\text{F}_5)_3$ via cationic intermediates. *Angew. Chem. Int. Ed.* 56, 11995–11999
2. Voss, T. et al. (2010) Cyclizations via frustrated Lewis pairs: Lewis acid induced intramolecular additions of amines to olefins and alkynes. *Chem. Eur. J.* 16, 3005–3008
3. Melen, R.L. (2014) Application of pentafluorophenyl boron reagents in the synthesis of heterocyclic and aromatic compounds. *Chem. Commun.* 50, 1161–1174
4. Wilkins, C.L. et al. (2016) Lewis acid-base 1,2-addition reactions: synthesis of pyrylium borates from enynoate precursors. *Dalton Trans.* 45, 5929–5932
5. Tamke, S. et al. (2016) Frustrated Lewis pair-catalyzed cycloisomerization of 1,5-enynes via a 5-endo-dig cyclization/protodeborylation sequence. *Angew. Chem. Int. Ed.* 55, 4336–4339
6. Kehr, G. and Erker, G. (2016) Advanced 1,1-carboboration reactions with pentafluorophenylboranes. *Chem. Sci.* 7, 55–65
7. Melen, R.L. et al. (2013) Cyclisation versus 1,1-carboboration: reactions of $\text{B}(\text{C}_6\text{F}_5)_3$ with propargyl amides. *Chem. Eur. J.* 19, 11928–11938
8. Wilkins, C.L. et al. (2015) Pathways to functionalized heterocycles: propargyl rearrangement using $\text{B}(\text{C}_6\text{F}_5)_3$. *Organometallics* 34, 5298–5309
9. Chen, C. et al. (2013) Dibenzopentalenes from $\text{B}(\text{C}_6\text{F}_5)_3$ -induced cyclization reactions of 1,2-bis(phenylethynyl)benzenes. *Angew. Chem. Int. Ed.* 52, 5992–5996